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APPLICATION NO. 8	FILING DATE / 97	BO TIME FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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MORRISON AND FOERSTER
2000 PENNSYLVANIA AVENUE N W
WASHINGTON DC 20006

HM12/0518

EXAMINER

SPECTOR, L

ART UNIT	PAPER NUMBER
1646	11

DATE MAILED: 05/18/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

Applicant(s)

Examiner

Group Art Unit

--The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address--

Period for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

Responsive to communication(s) filed on 3/24/99.

This action is FINAL.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

Claim(s) 1-40 is/are pending in the application.

Of the above claim(s) 2, 10, 12, 20, 22, 30, 32, 40 remain ~~is/are~~ withdrawn from consideration.

Claim(s) _____ is/are allowed.

Claim(s) 1, 3-9, 11, 13-19, 21, 23-29, 31, 33-39 is/are rejected.

Claim(s) _____ is/are objected to.

Claim(s) 1-40 ~~coincide~~ ~~are~~ subject to restriction or election requirement.

Application Papers

- See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- The proposed drawing correction, filed on _____ is approved disapproved.
- The drawing(s) filed on _____ is/are objected to by the Examiner.
- The specification is objected to by the Examiner.
- The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- All Some* None of the CERTIFIED copies of the priority documents have been received.
- received in Application No. (Series Code/Serial Number) _____.
- received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Attachment(s)

- Information Disclosure Statement(s), PTO-1449, Paper No(s). _____ Interview Summary, PTO-413
- Notice of References Cited, PTO-892 Notice of Informal Patent Application, PTO-152
- Notice of Draftsperson's Patent Drawing Review, PTO-948 Other _____

Office Action Summary

Part III: Detailed Office Action

Species Election Requirement:

Applicants argument pertaining to the non-elected species is inapposite at this time, as the generic claims have not been indicated as being allowable.

5 It is noted that applicants requested in the interview held 3/19/99 that the Examiner review the applicability of the restriction requirement made in the application of U.S. Patent Number 4,751,180 to the current case. The Examiner has reviewed that file and has found that the restriction requirement therein has no applicability to this case on the grounds that there are no common inventors, no priority claimed to that case, and the subject matter currently claimed does not appear 10 therein. Applicants are reminded that restriction is not required, but is made at the discretion of the Examiner on the basis that the inventions being restricted can support separate patents, and present a burdensome search. It is the Examiner's position in this case that as recombinant DNA technology is the only practical way to make the claimed proteins, that restriction would not be proper.

15 **Formal Matters:**

The rejection of claims under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of copending Application No. 08/853524 in view of Thomason, Reddy-1 and Reddy-2 is withdrawn in view of the abandonment of the copending application.

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25 The language "partial CTP unit or variant thereof", such as appears in claim 6, is not limiting as concerns any particular amino acid sequence. The specification as filed has no clear definition of a "partial CTP unit". As there is no functional limitation on such, nor any limitation on minimal length, the Examiner concludes that this definition includes any "partial CTP unit" which is as short as a dipeptide, such being the shortest possible "sequence" of amino acids. The claim includes not only all such "partial CTP" units, but "variant thereof". A variant being a sequence having one or more substitutions, it follows that a "variant" of a "partial CTP unit", when read in light of the

specification, may have no sequence nor property in common with a CTP unit. As such, those sequences falling within the metes and bounds of such language are not limited, and art will be applied accordingly. Applicants have argued that the partial CTP must contain at least one glycosylation site. This argument has been fully considered but is not deemed persuasive because the specification
5 merely states that such is a 'preferable' embodiment; the limitation cannot be read into the claims.

Rejections Over Prior Art:

10 The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

15 (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

20 This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

25 Claims 1, 4, 8, 11, 14, 18, 21, 24, 28, 31, 34 and 38 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Thomason, U.S. Patent number 5,705,484 in view of Reddy et al., WO 85/01959, (Reddy-1) cited by applicants, and U.S. Patent number 4,923,805, also to Reddy et al. (Reddy-2) for reasons cited in the previous Office Action, paper number 8 mailed 12/21/98, at page(s) 5-6. Applicants arguments filed 3/24/99 have been fully considered but are not deemed
30 persuasive. Applicants argue that just as the monellin disclosure was not "patent-defeating" as to PDGF as claimed by Thomason, Thomason should not be 'defeating' of the glycoprotein hormones. This argument has been fully considered but is not deemed persuasive because there is no evidence

of record that the monellin references were considered in prosecution of the Thomason patent, and the Thomason patent is not and will not be subject to reexamination herein. The Examiner in this case has cited the Thomason patent as being the *closest*, not the *only* applicable prior art. Thomason was considered by the Examiner to be the closest prior art because like PDGF, the glycoprotein hormones are dimeric molecules that have hormone/growth factor activity (both are soluble molecules that influence the physiology of target cells by binding to specific receptors thereon). As stated in the rejection, the person of ordinary skill in the art would have been motivated substitute glycoprotein hormone subunits such as disclosed by Reddy et al. in the constructs of Thomason due to the disclosed advantages of such as pointed out by Thomason, namely favorable renaturation kinetics and stability. One of ordinary skill in the art would immediately have recognized, upon reading Thomason's disclosure that the method would be reasonably expected to be successful for any dimeric protein, with or without a linker sequence, as disclosed by Thomason.

Applicants attempt to make much of the fact that the PDGF dimers made in single chain form by Thomason are disulfide bonded proteins, whereas the glycoprotein hormones are not. The Examiner does not disagree with the facts, but comes to a much different conclusion. The Examiner's position is that the person of ordinary skill in the art would immediately recognize, upon reading Thomason's disclosure that if it was advantageous to make dimeric proteins which are normally held together by stable covalent bonds in single chain form, and if that single chain form conferred advantages as disclosed by Thomason such as favorable renaturation kinetics and increased stability, that to do so with a dimeric protein that was normally held together by less stable, non-covalent interactions would be even *more* desirable, that is, the advantages cited by Thomason would be even more desirable and pronounced when the method was applied to such proteins.

The Examiner does not agree with the assertion at page 8 of Applicants response that "applicants field of endeavor is in the glycoprotein hormones, and especially the three gonadotropins." The Examiner finds this to be an unduly restrictive view of applicant's field, in that the invention clearly requires knowledge and proficiency in the art of molecular biology in general, and recombinant DNA technology. It is not consistent with practice in the art to posit that only

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with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

5 Official papers filed by fax should be directed to (703) 305-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Please advise the Examiner at the telephone number above when an informal fax is being transmitted.


Lorraine Spector, Ph.D.
Primary Examiner

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U.S. Patent number 4,751,180 for reasons cited in the previous Office Action, paper number 8 mailed 12/21/98, at page(s) 8. Applicants arguments filed 3/24/99 have been fully considered but are not deemed persuasive for reasons cited above.

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Advisory Information:

No claim is allowed.

10 **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

15 A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

20 Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 8:00 A.M. to 4:30 P.M.

25 If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Paula Hutzell, Ph.D., can be reached at (703)308-4310.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

30 Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform

would only be familiar with molecular biology or recombinant DNA technology as it applies to a single protein or group of proteins. It is widely accepted in the art that techniques that are practiced with one nucleic acid or protein sequence can be readily adapted to others. It remains that Thomason made a single chain pseudo dimer with PDGF, and that the person of ordinary skill in the art would immediately have recognized on the basis of Thomason's disclosure that it would be desirable to extend Thomason's teachings to other dimeric proteins which transmit signals to cells via receptor binding, such as the glycoprotein hormones taught by Reddy et al.

10 Claims 7, 9, 17, 19, 27, 29, 37 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomason, U.S. Patent number 5,705,484 in view of Reddy et al., WO 85/01959, (Reddy-1) cited by applicants, and U.S. Patent number 4,923,805, also to Reddy et al. (Reddy-2) as applied to claims 1, 4, 8, 11, 14, 18, 21, 24, 28, 31, 34 and 38 above, and further in view of Zurawski et al., EMBO Journal 7(4):1061-1069, 1988 for reasons cited in the previous Office Action, 15 paper number 8 mailed 12/21/98, at page(s) 6-7. Applicants arguments filed 3/24/99 have been fully considered but are not deemed persuasive for reasons cited above.

20 Claims 3, 6, 13, 36, 23, 26, 33 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomason in view of Reddy-1 and Reddy-2 as applied to claims 1, 4, 8, 11, 14, 18, 21, 24, 28, 31, 34 and 38 above, and further in view of Fares et al., cited by applicants, or Boime, U.S. Patent number 5,585,345 for reasons cited in the previous Office Action, paper number 8 mailed 12/21/98, at page(s) 7-8. Applicants arguments filed 3/24/99 have been fully considered but are not deemed persuasive for reasons cited above.

25 Claims 5, 15, 25 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomason in view of Reddy-1 and -2 as applied to claims 1, 4, 8, 11, 14, 18, 21, 24, 28, 31, 34 and 38 above, and further in view of Chaudhary et al., Nature 339:394, June 1989 and Cousens et al.,